FIG. 1A

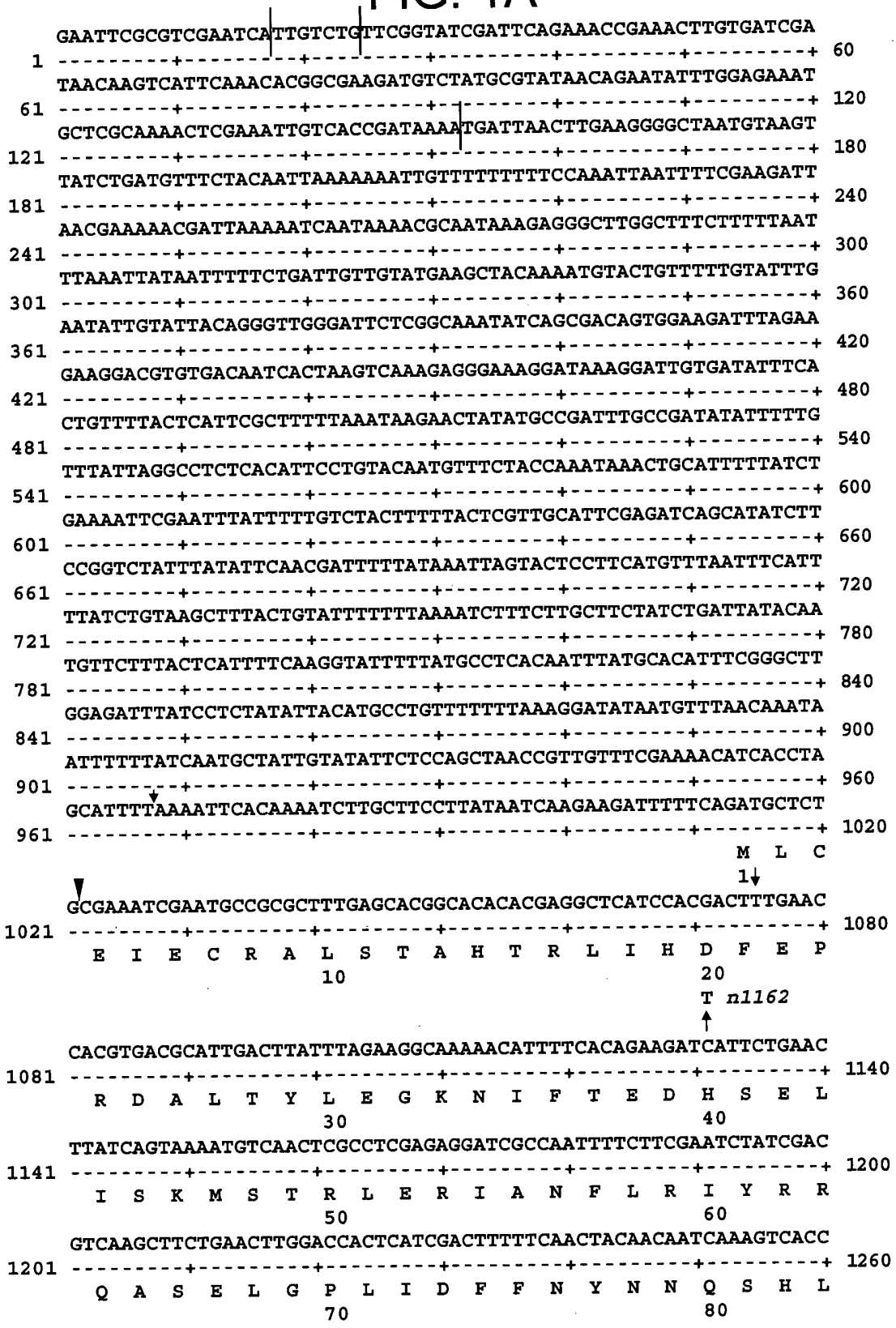

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FIG. 1B

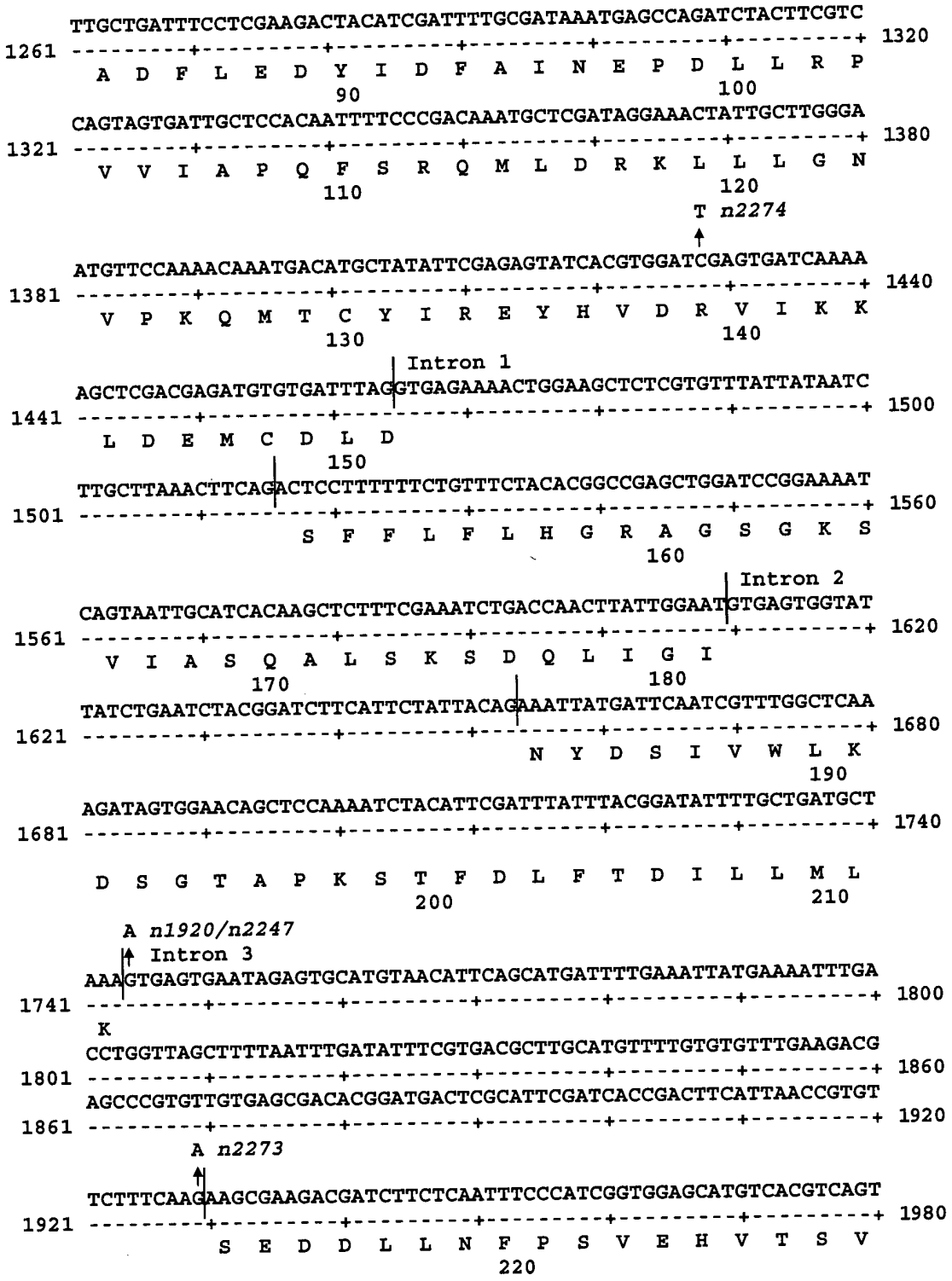

FIG. 1C

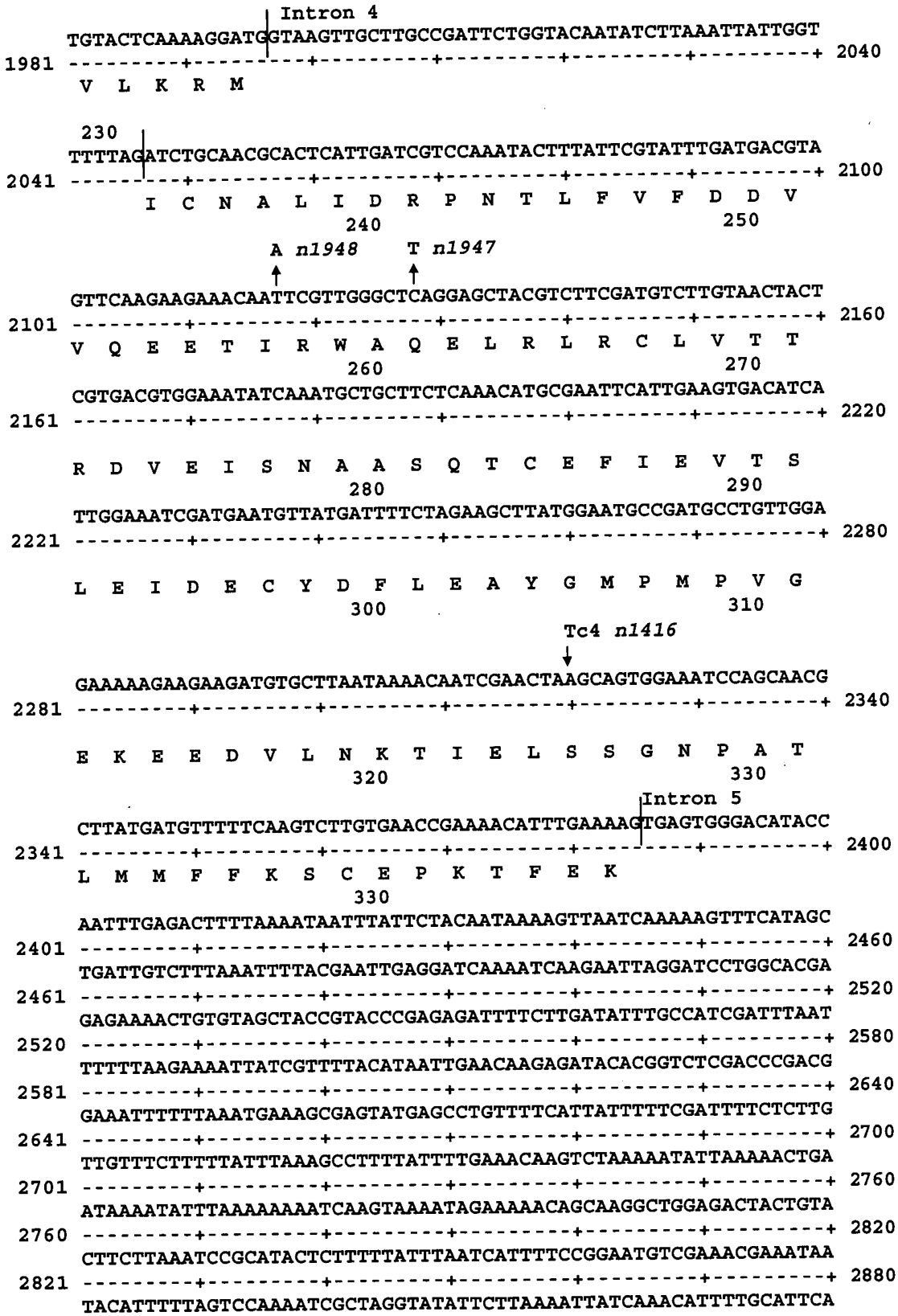

FIG. 1D

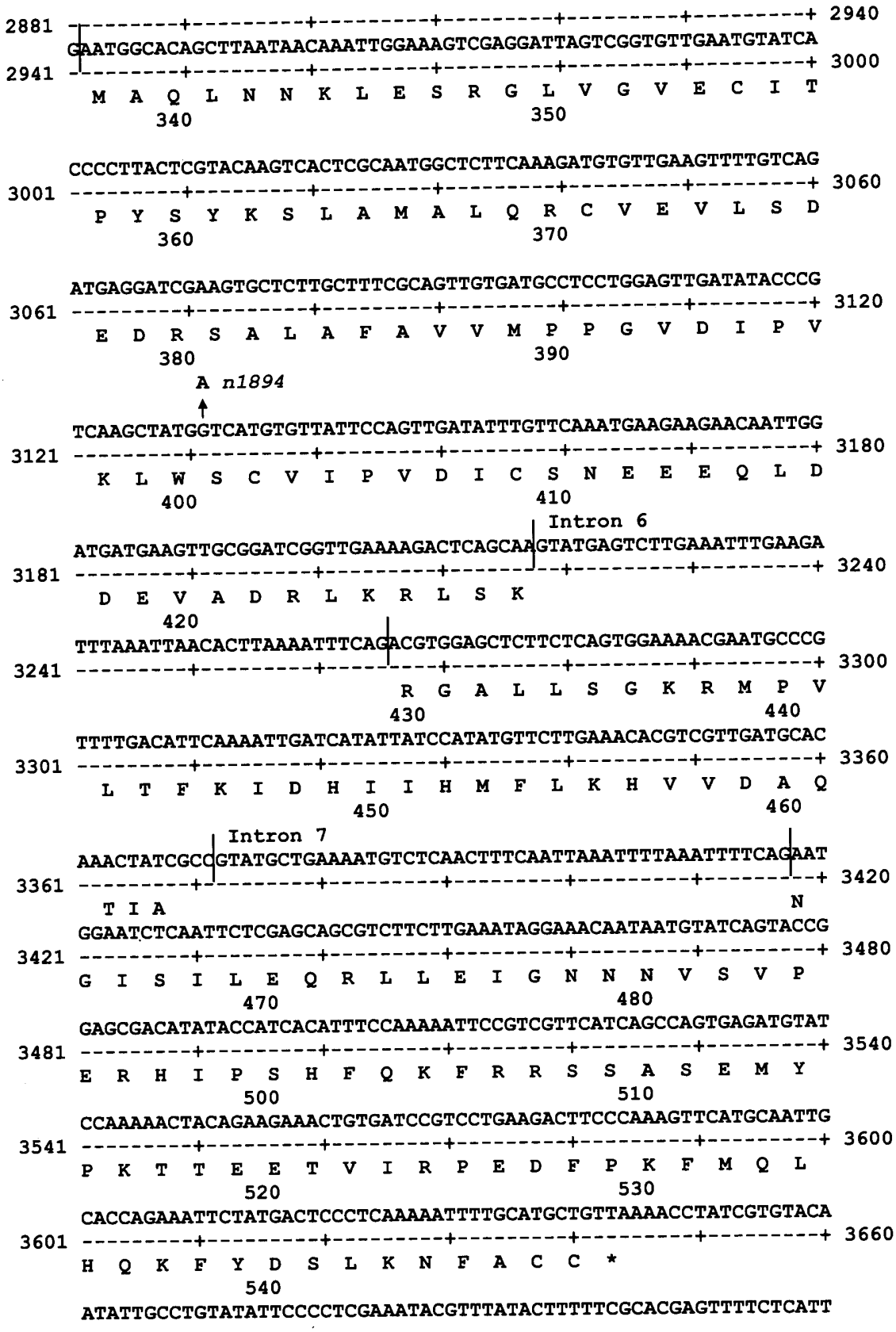

FIG. 1E

```
3661 ---------+---------+---------+---------+---------+---------+ 3720
     TTTTCATTTGTACTTGTTTTATTTCTCTCCAAAATTTCAGATCTATCCCAAATGTTCTTA
3721 ---------+---------+---------+---------+---------+---------+ 3780
     AATTTAATGTTTTCTACAGATACTCAACACATCTTGTTTCATCTCATCCTTGCTTTTTTT
3781 ---------+---------+---------+---------+---------+---------+ 3840
     TTTCAAATATATTCAGTTTCTTTTATAATTTTAATTAATCGAATTAATACATTCACGTAA
3841 ---------+---------+---------+---------+---------+---------+ 3900
     AGAATTTCGTGGACTATTATTTTATCGCATCCAAATGATTTATTCCCTATTGTTCGAAAC
3901 ---------+---------+---------+---------+---------+---------+ 3960
     TTCCAAATTGATCATTTTTAAACACGCCTCATTAAATTGAAAGTCGTACTTTTAGTCTCG
3961 ---------+---------+---------+---------+---------+---------+ 4020
     AACATGAAGTAAGTTATTTTCTGTGTTCTAAATTCAAAGTGCATTCCAAAAGGACATTTG
4021 ---------+---------+---------+---------+---------+---------+ 4080
     ATGAGTTTTCACGAAAACCGTAATTTTTACAATTTCCTTTCAGTTTTGAAGATGTTCGAT
4081 ---------+---------+---------+---------+---------+---------+ 4140
     TTCTTTCCTCTGTTGGCGTCATTACTACATTTGCTTTGCTGCTTCACTTTATCGAGATTC
4141 ---------+---------+---------+---------+---------+---------+ 4200
     TTGCCATCAATGGAGTTCCATCTAGACCGATAGCAGTCTTCATATCATTATCCCTGTATA
4201 ---------+---------+---------+---------+---------+---------+ 4260
     TTGTACTGTTTCAGTATTTTAACTTATCGATTACGTACTATATTCAGTGGTTCACTGTTT
4261 ---------+---------+---------+---------+---------+---------+ 4320
     TCGGTCAATGGGTGACACGTGCTCGACGANNAATTTTCAACGAACGCAATCTCCTAGTCA
4320 ---------+---------+---------+---------+---------+---------+ 4380
     CTTATCAACCAAGAGCCCTCACCCATG
4380 ---------+---------+------- 4407
```

FIG. 2

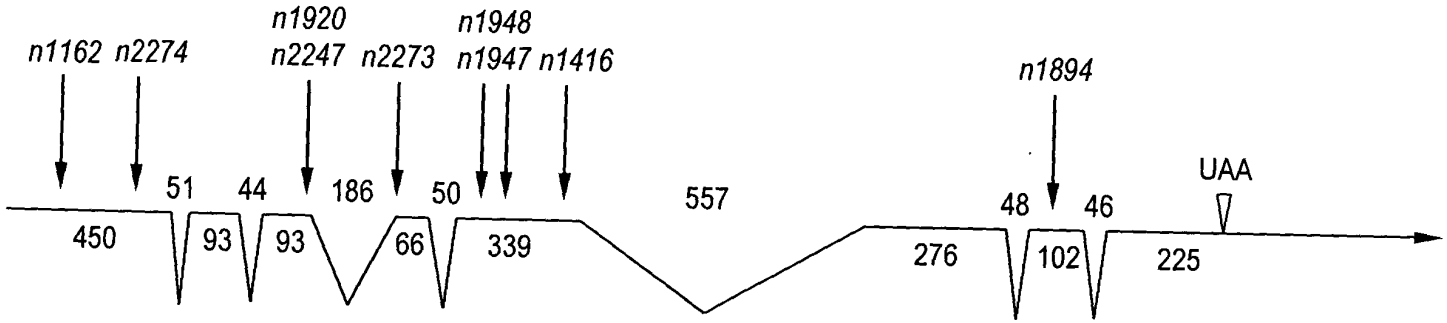

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FIG. 3

	10	12	14	18	21
	X	Y	Z	-X	-Z
Calcium-binding loop concensus	D	N	S	T	E
		D	N	S	
			D	E	
				Q	
				D	
				N	
EF-hand consensus	O	*	O	*	O	G	*	*	O	*	*	E
ced-4 sequence 1	Y	N	**N**	Q	**S**	H	L	A	**D**	F	L	**E**
sequence 2	S	L	E	I	**D**	E	C	Y	**D**	F	L	**E**
Parvalbumin (carp)	**D**	Q	**D**	K	**S**	**G**	F	I	**E**	E	D	**E**
(hake)	**D**	Q	**D**	K	**D**	D	F	I	G	E	D	**E**
(ray)	**D**	S	**D**	G	**D**	H	K	I	G	V	D	**E**
SCBP (*Amphioxus I*)	**D**	I	**N**	K	**D**	D	V	V	**S**	W	E	E
ICaBP (bovine)	A	K	E	G	**D**	P	Q	L	**S**	K	E	E
	D	K	**N**	G	**D**	**G**	E	V	**S**	F	E	E
Troponin C (rabbit)	**D**	A	**D**	G	G	**G**	D	I	**S**	V	K	**E**
	D	E	**D**	G	**S**	**G**	T	I	**D**	F	E	**E**
	D	R	**N**	A	**D**	**G**	Y	I	**D**	A	E	**E**
	D	K	**N**	N	**D**	**G**	R	I	**D**	F	D	**E**
Calmodulin (bovine)	**D**	K	**D**	G	**N**	**G**	T	I	T	T	K	**E**
Trypsinogen	L	G	E	D	**N**	I	N	VV	**E**	G	N	**E**
Fibrinogen	**D**	N	**D**	N	**D**	K	F	EG	**N**	C	A	**E**
Villin	G	V	**D**	P	**S**	R	K	E	**N**	H	L	**S**
GBP	D	L	**N**	K	**D**	G	Q	I	**Q**	_	I	**E**

FIG. 4A

ced-3 Genomic Sequence

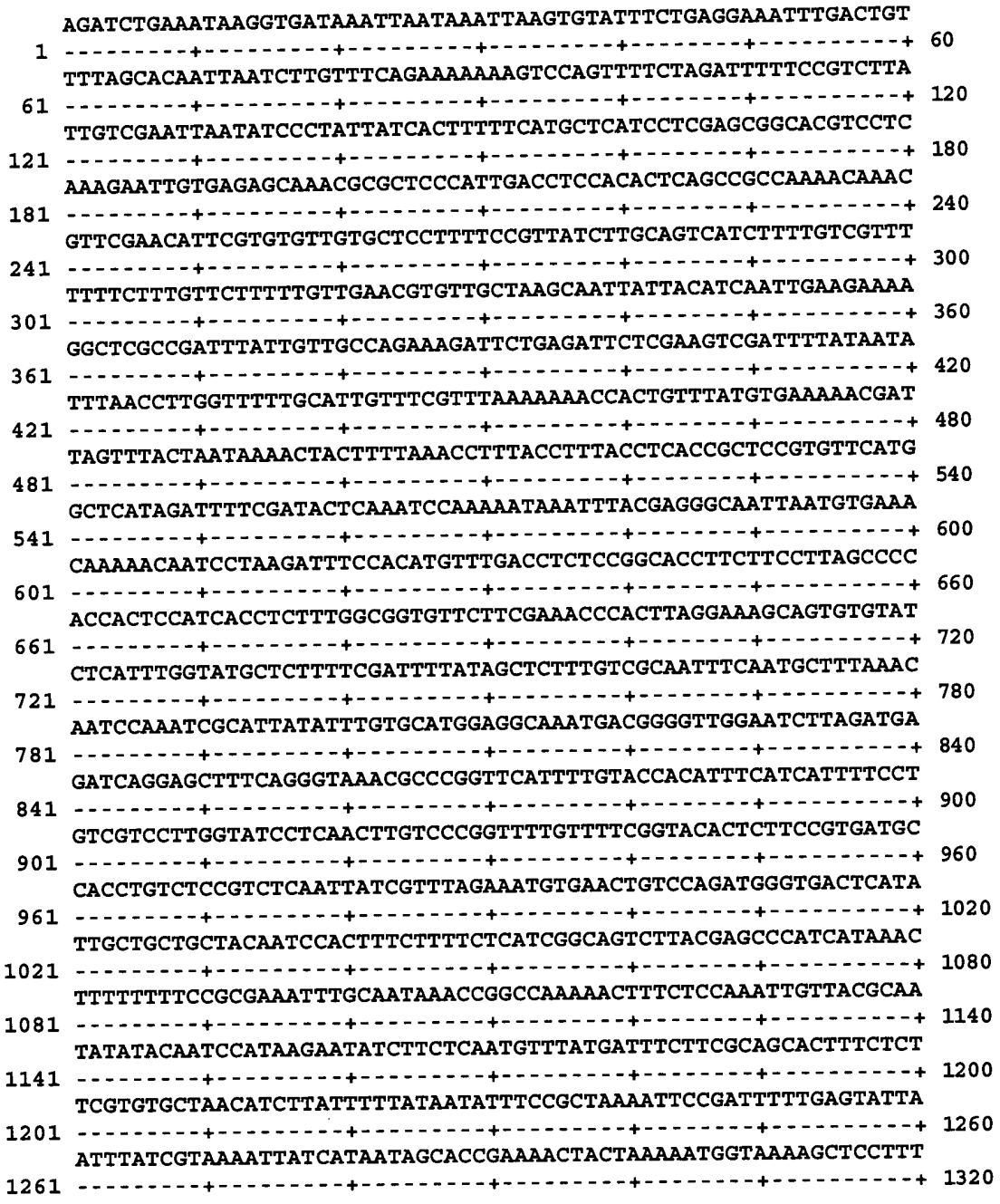

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FIG. 4B

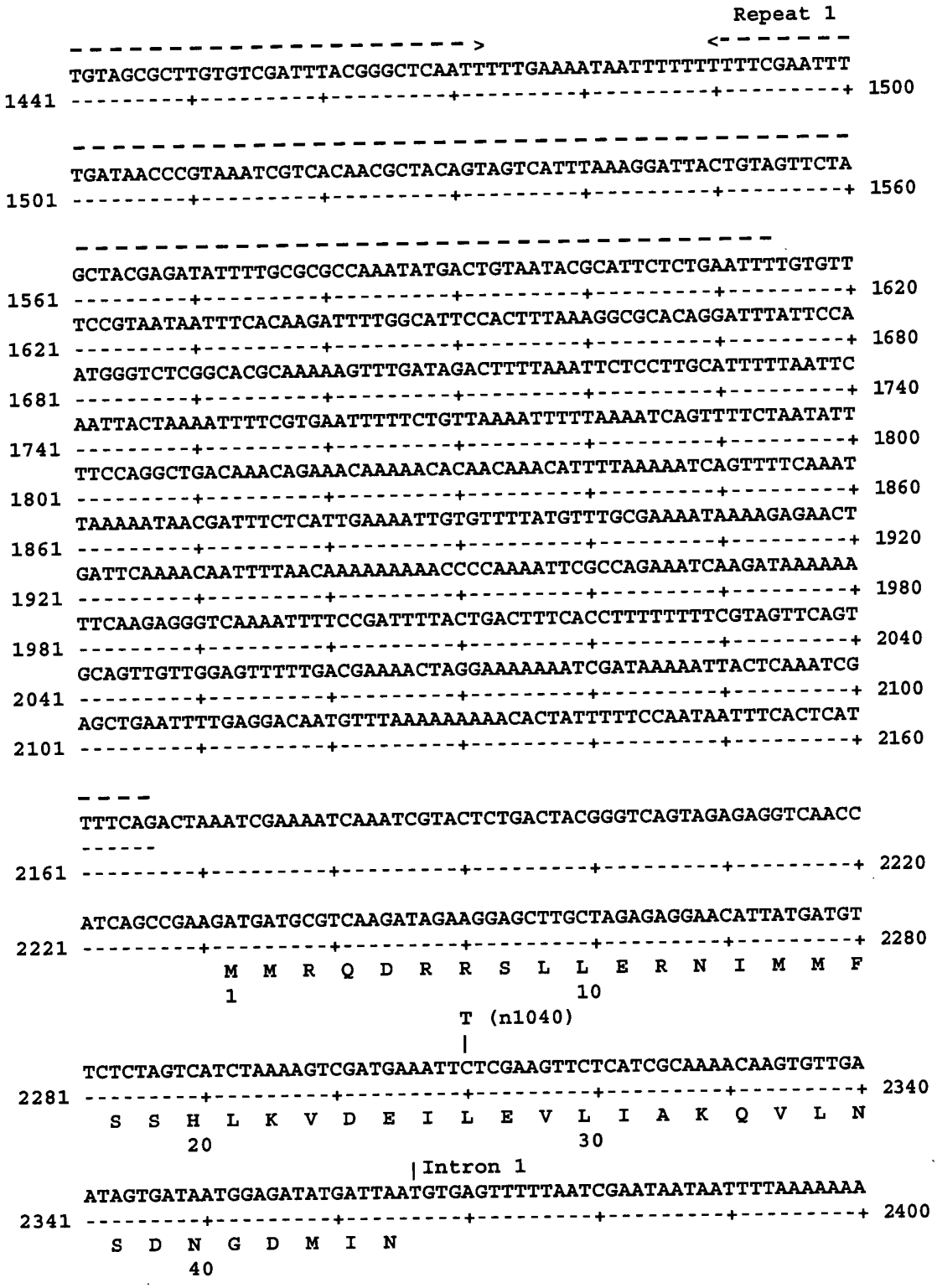

FIG. 4C

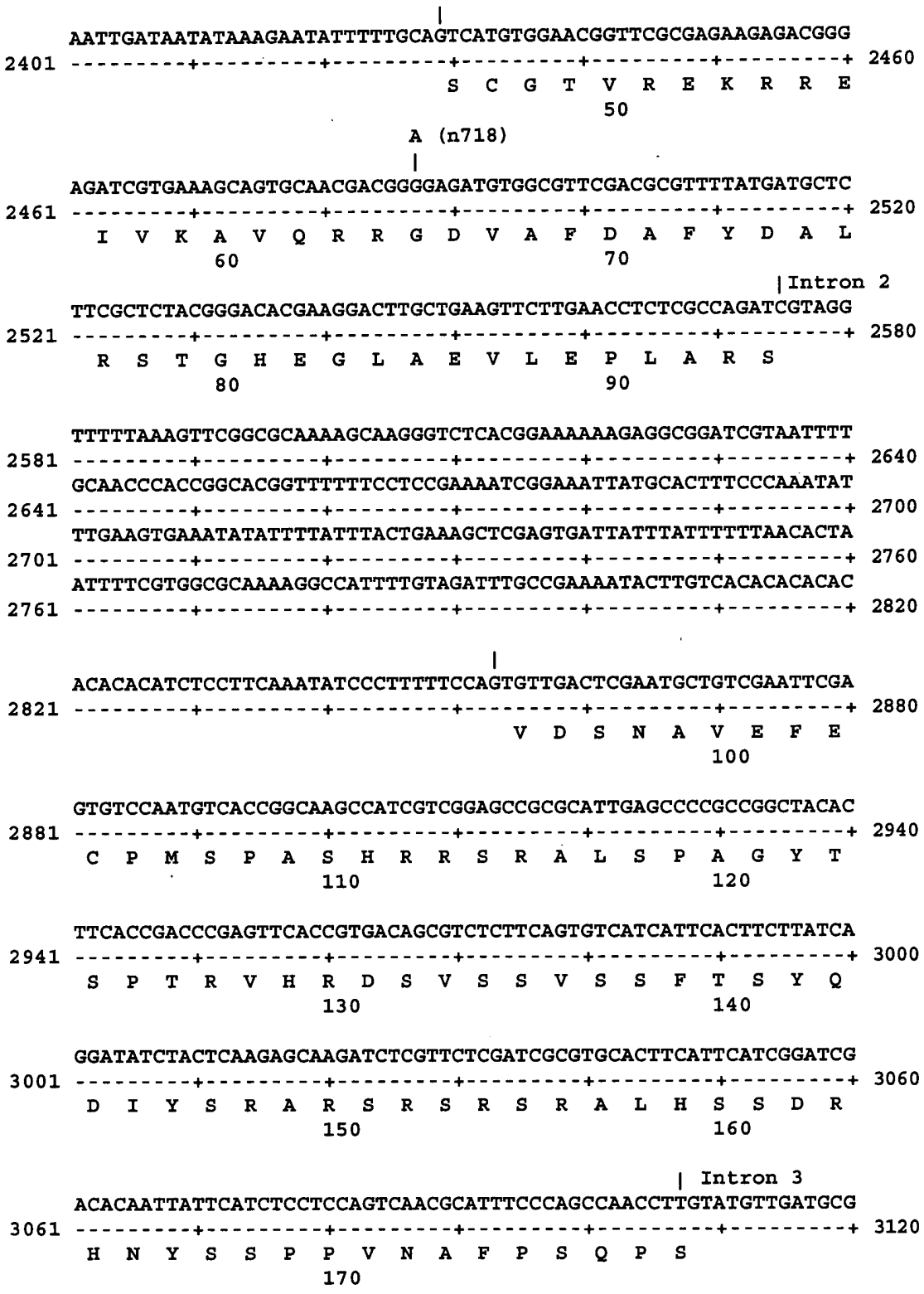

FIG. 4D

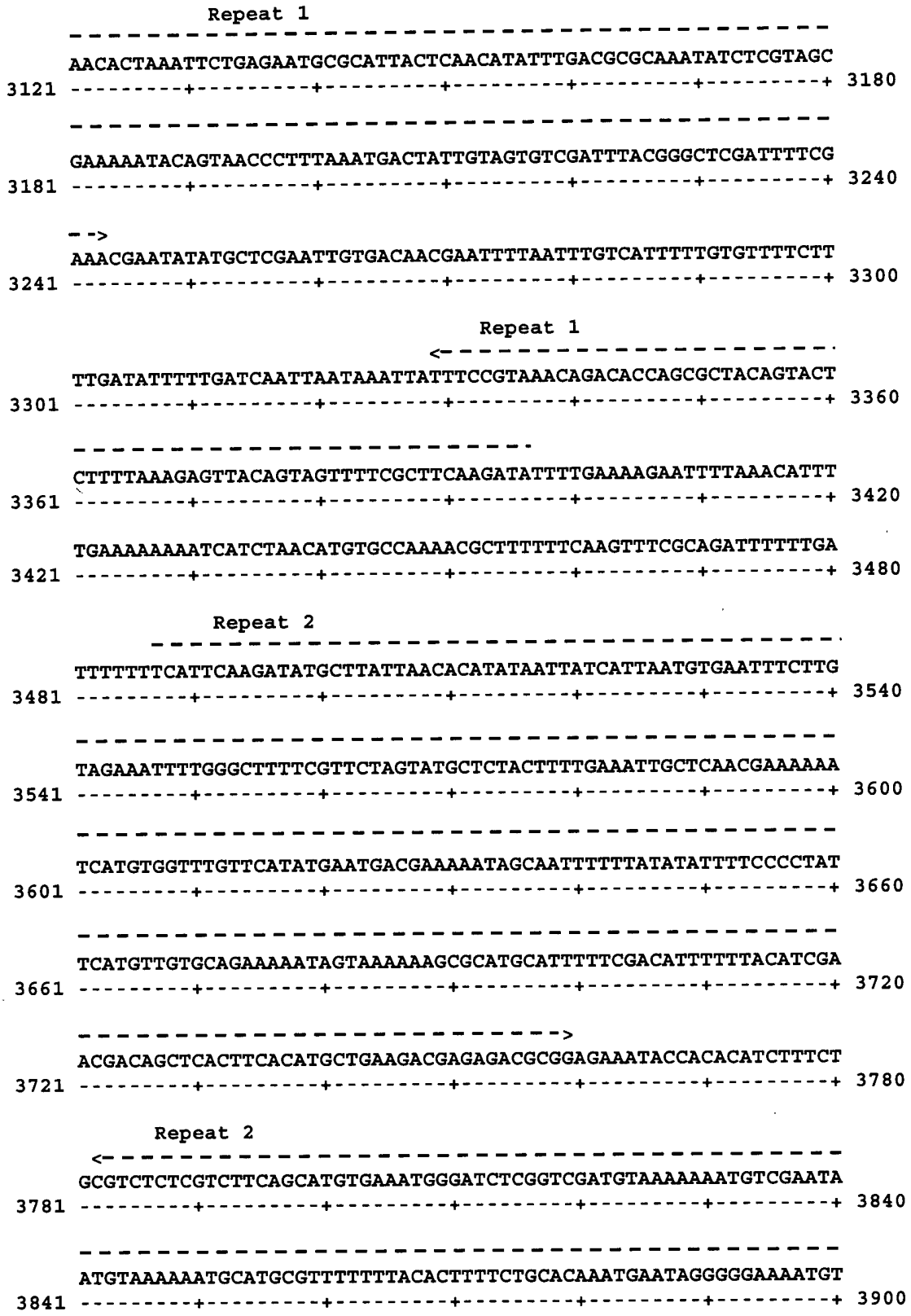

FIG. 4E

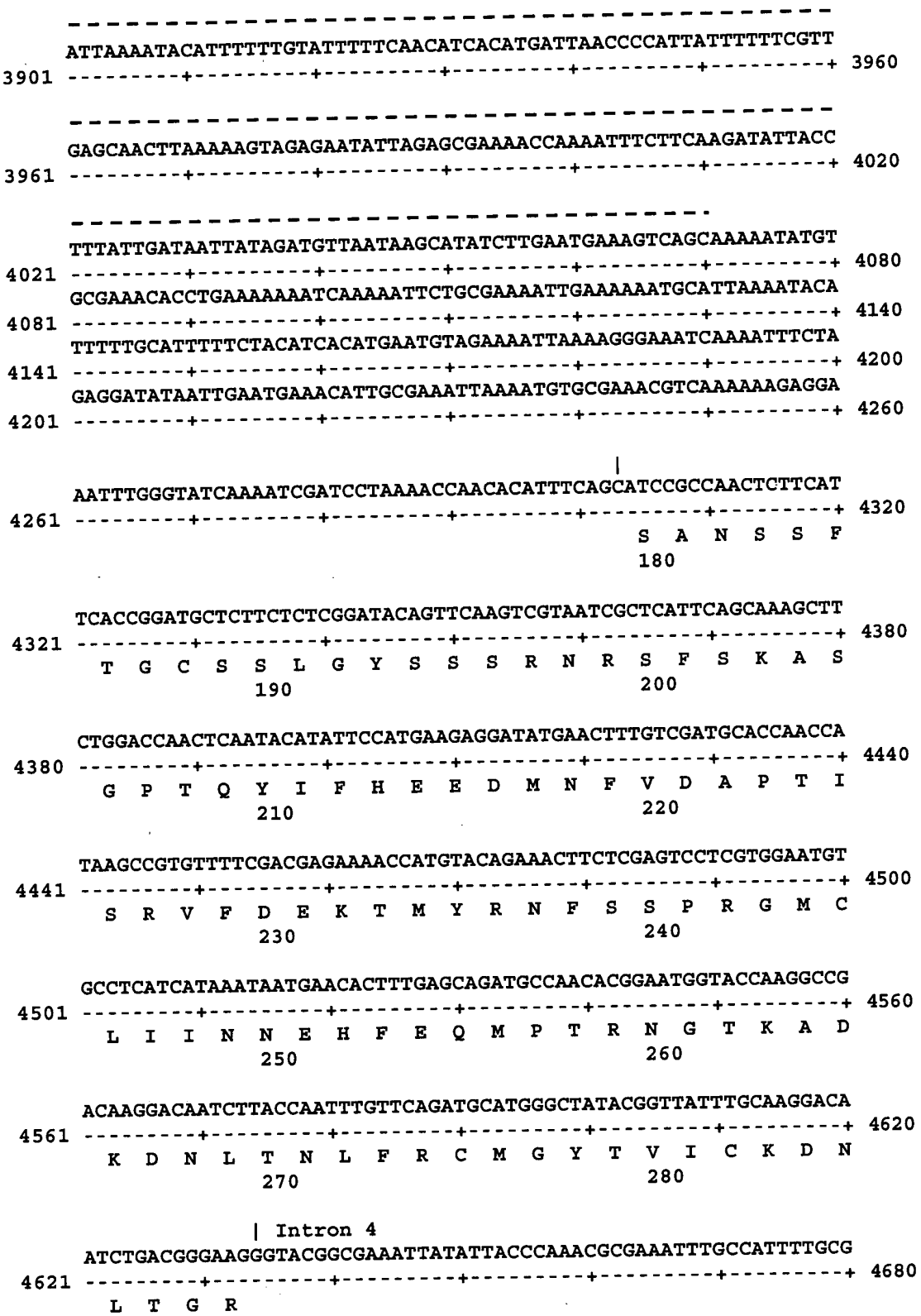

FIG. 4F

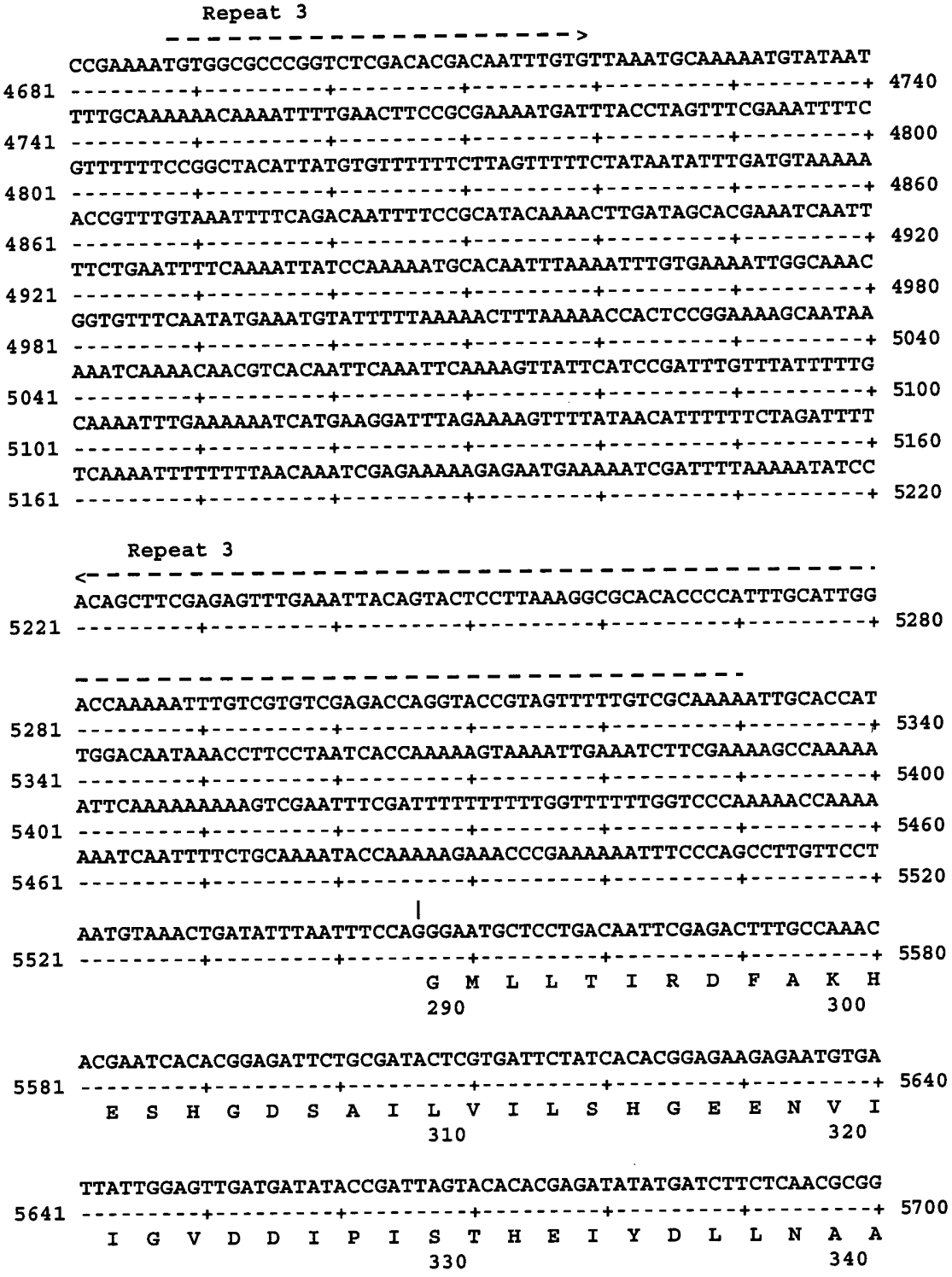

FIG. 4G

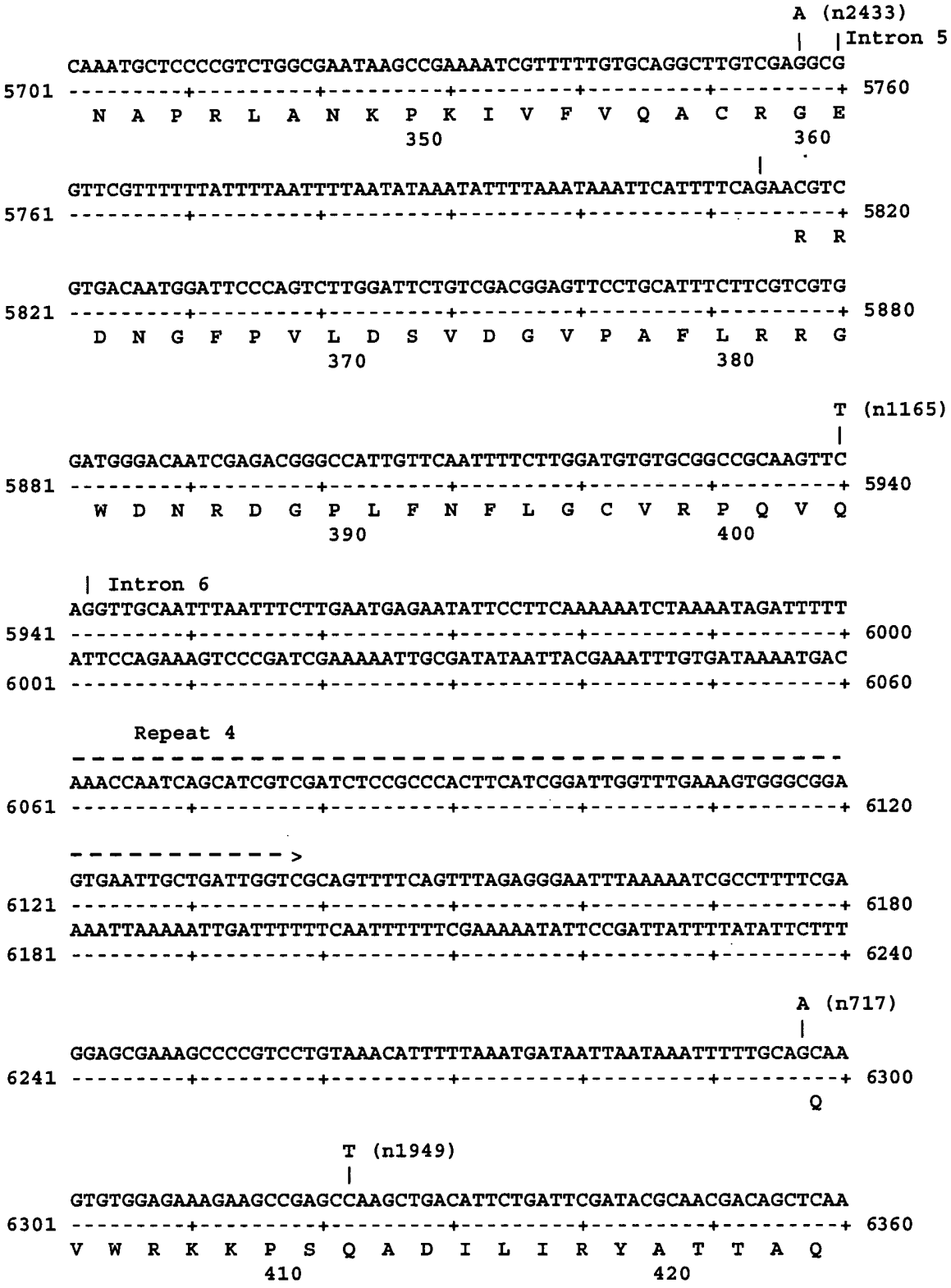

FIG. 4H

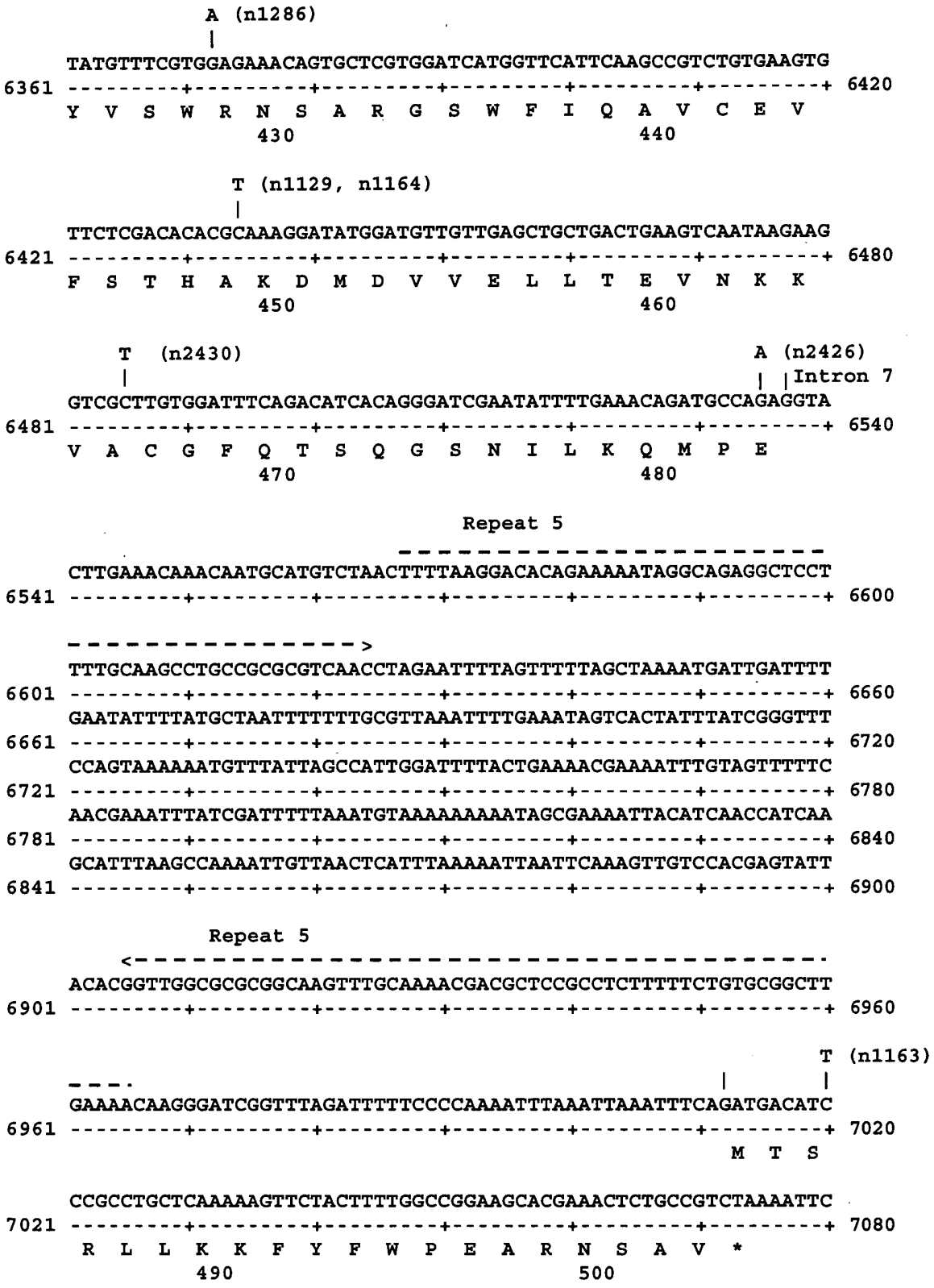

FIG. 4I

```
     ACTCGTGATTCATTGCCCAATTGATAATTGTCTGTATCTTCTCCCCCAGTTCTCTTTCGC
7081 ---------+---------+---------+---------+---------+---------+ 7140
     CCAATTAGTTTAAAACCATGTGTATATTGTTATCCTATACTCATTTCACTTTATCATTCT
7141 ---------+---------+---------+---------+---------+---------+ 7200
     ATCATTTCTCTTCCCATTTTCACACATTTCCATTTCTCTACGATAATCTAAAATTATGAC
7201 ---------+---------+---------+---------+---------+---------+ 7260
     GTTTGTGTCTCGAACGCATAATAATTTTAATAACTCGTTTTGAATTTGATTAGTTGTTGT
7261 ---------+---------+---------+---------+---------+---------+ 7320
     GCCCAGTATATATGTATGTACTATGCTTCTATCAACAAAATAGTTTCATAGATCATCACC
7321 ---------+---------+---------+---------+---------+---------+ 7380
     CCAACCCCACCAACCTACCGTACCATATTCATTTTTGCCGGGAATCAATTTCGATTAATT
7381 ---------+---------+---------+---------+---------+---------+ 7440
     TTAACCTATTTTTTCGCCACAAAAAATCTAATATTTGAATTAACGAATAGCATTCCCATC
7441 ---------+---------+---------+---------+---------+---------+ 7500
     TCTCCCGTGCCGGAATGCCTCCCGGCCTTTTAAAGTTCGGAACATTTGGCAATTATGTAT
7501 ---------+---------+---------+---------+---------+---------+ 7560
     AAATTTGTAGGTCCCCCCCATCATTTCCCGCCCATCATCTCAAATTGCATTCTTTTTTCG
7561 ---------+---------+---------+---------+---------+---------+ 7620
     CCGTGATATCCCGATTCTGGTCAGCAAAGATCT
7621 ---------+---------+---------+--- 7653
```

FIG. 5A

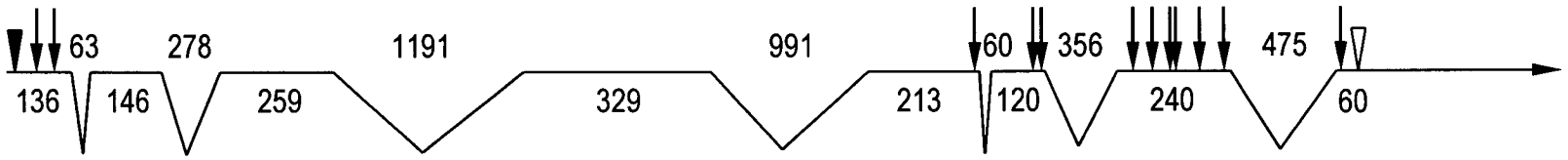

FIG. 5B

ced-3 Mutations are Clustered

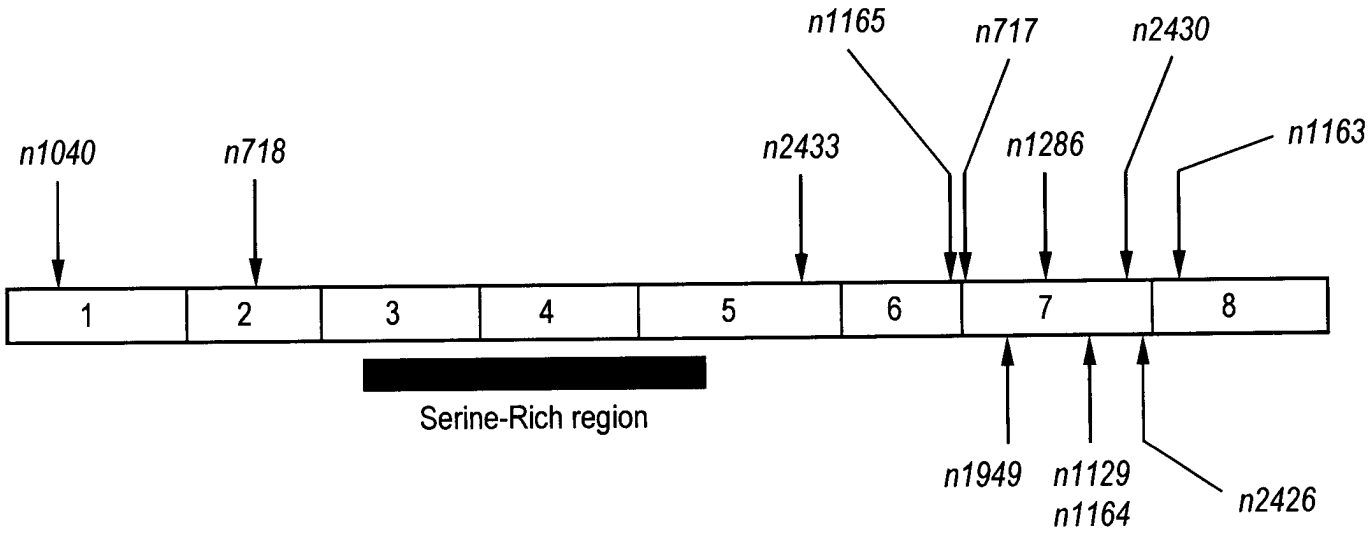

FIG. 6

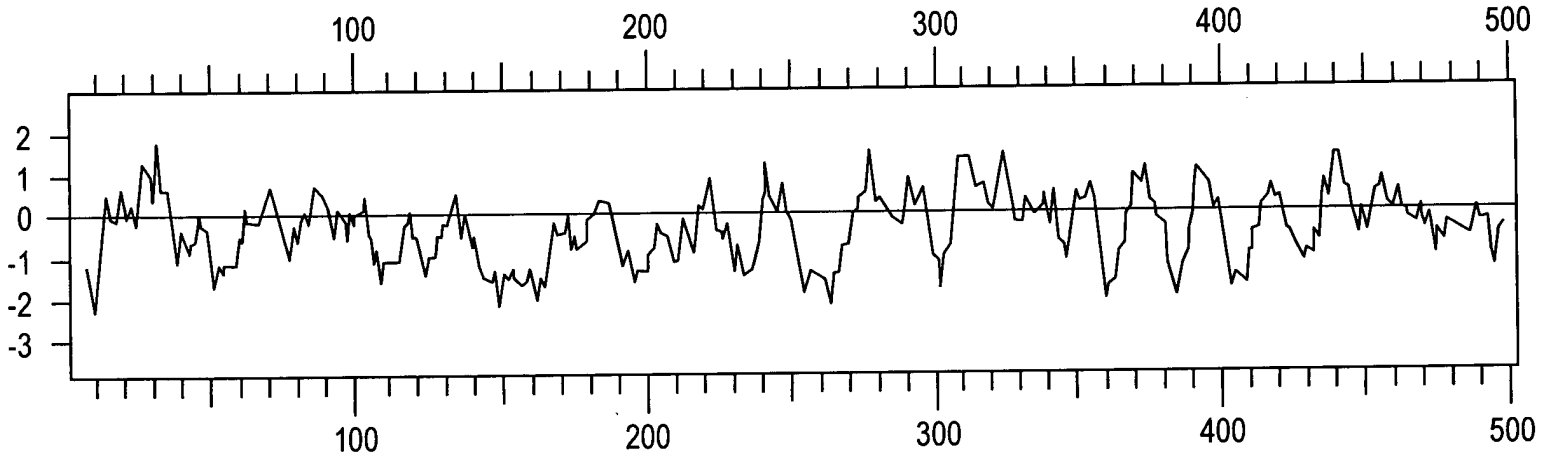

FIG. 7

```
Lines
  1   01 MMRQDRRSLLERNIMMFSSHLKVDEILEVLIAKQVLNSDNGDMINSCGTV 50
  2      ......W_......LE...K.QA.L..D.............V....R.E
  3                              TVS.SLI..R.......  M.....

  1   51 REKRREIVKAVQRPGDVAFDAFYDALRSTGHEGLAEVLEPLARSVDSNAV 100
  2      .DNEK........R..E..........D...ND..D..M..S.P     .P.
  3

  1  101 EFECPMSPASHRRSRALSPAGYTSPTRVHRDSVSSVSSFTS_YQDIYSRA 149
  2      PM......S..........P .A.........I.........T...V....
  3                                                       S

  1  150 RSRSR_SRALHSSDRHNYSSPPVNAFPSQPSSANSSFTGCSSLGYSSSRN 198
  2      ..S..S..P.Q.......M.AA_TS..... .........A.........
  3      T..._..P..T......V..S_.S.Q...A........S.........T

  1  199 RSFSKASGPTQYIFHEEDMNFVDAPTISRVFDEKTMYRNFSSPRGMCLI  247
  2      .....T.AQS..........Y......H................L...
  3      ..Y....AHS..........Y......H.............T...L...

  1  248 INNEHFEQMPTRNGTKADKDNLTNLFRCMGYTVICKDNLTGRGMLLTIRD 297
  2      ........................I..................E..S...S
  3      ................P....IS........I.H........ .M.....


  1  298 FAKHESHGDSAILVILSHGEENVIIGVDDIPISTHEIYDLLNAANAPRLA 347
  2      .GRNDM.............. ........VSVNV.................
  3      ...N.T..... ................VSVNV....X............

  1  348 NKPKIVFVQACRGERRDNGFPVLDSVDGVPAFLRRGWDNRDGPLFNFLGC 397
  2      ....L.........................SLI..................
  3      ....L............V.............LI.....KG...  .....


  1  398 VRPQVQQVWRKKPSQADILIRYATTAQYVSWRNSARGSWFIQAVCEVFST 447
  2      ................M..A............................L
  3      ....A..............A............................L

  1  448 HAKDMDVVELLTEVNKKVACGFQTSQGSNILKQMPEMTSRLLKKFYFWPE 497
  2      .....................................L.............
  3      ..........................A.......  L.............

  1  498 __ARN__SAV 503
  2      DRG..__...
  3      __D..RS...
```

Line 1 *C. elegans*
Line 2 *C. briggsae*
Line 3 *C. vulgaris*

FIG. 8

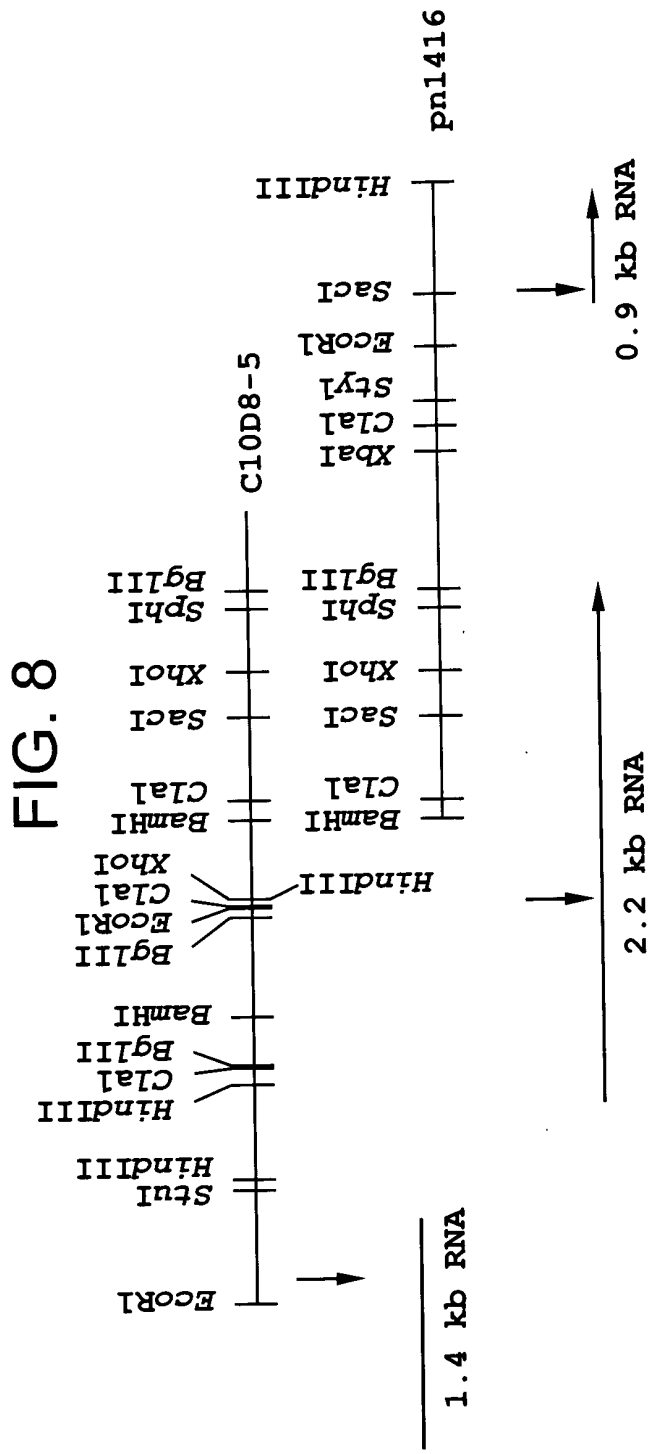

FIG. 9

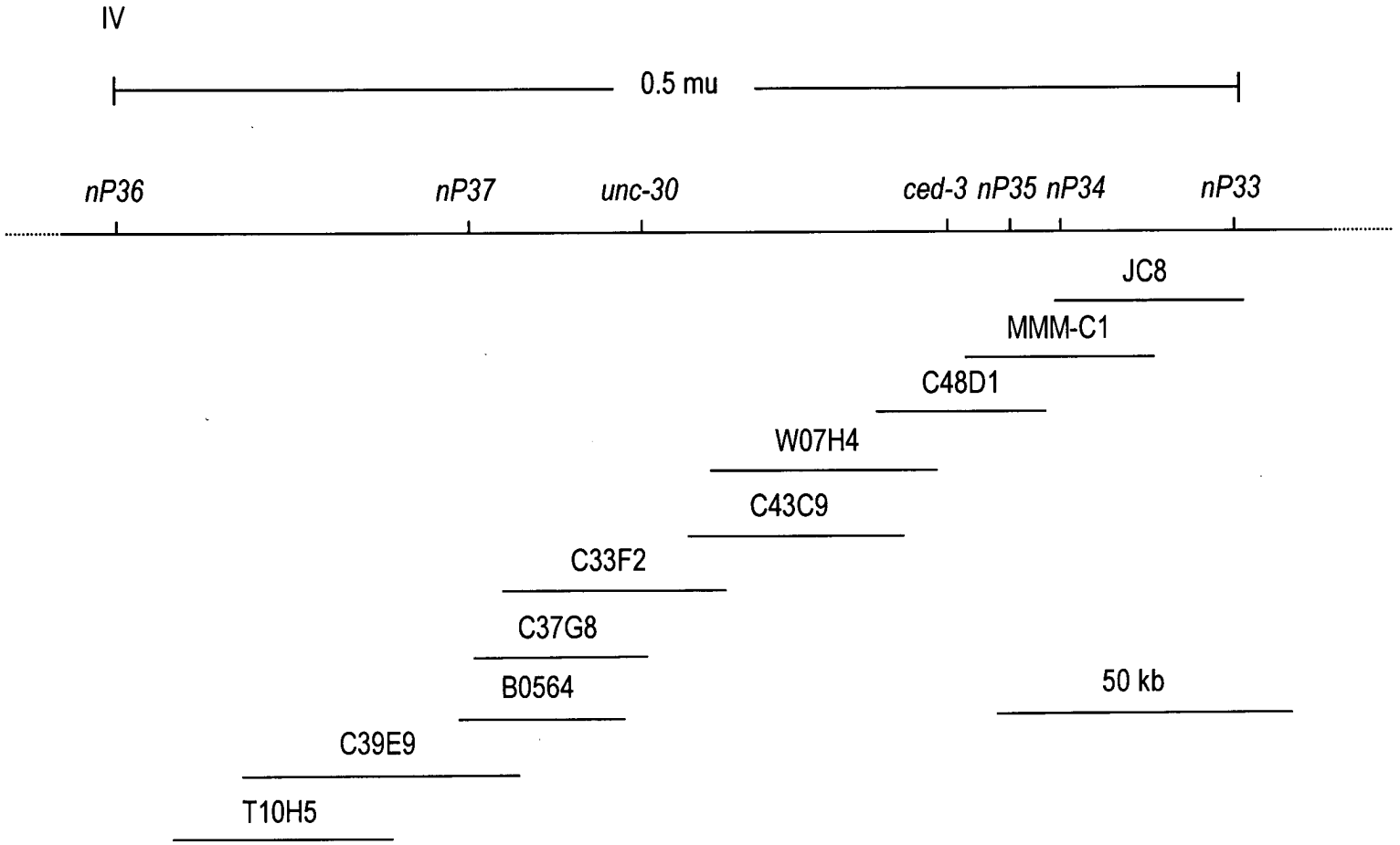

FIG. 10

Summary of the experiments to localize *ced-3* gene within C40D1